Constellation PHARMACEUTICALS

CPI-0610: Update of Preliminary Data from MANIFEST

Analyst/Investor Meeting on EHA Posters

Stellar Science, Breakthrough Medicine

June 12, 2020

Forward-Looking Statements

This presentation and discussion contain forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties, including statements regarding the implications of preliminary or interim clinical data, Company's plans, strategies and prospects for its business and statements regarding the development status of the Company's product candidates. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "will," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in, or implied by, such forward-looking statements. These risks and uncertainties include, but are not limited to, risks associated with the Company's ability to: obtain and maintain necessary approvals from the FDA and other regulatory authorities; continue to advance its product candidates in clinical trials; whether preliminary or interim data from a clinical trial will be predictive of the final results of the trial; replicate in later clinical trials positive results found in preclinical studies and early-stage clinical trials of CPI-0610, CPI-1205 and CPI-0209; advance the development of its product candidates under the timelines it anticipates, or at all, in current and future clinical trials; obtain, maintain, or protect intellectual property rights related to its product candidates; manage expenses; raise the substantial additional capital needed to achieve its business objectives; the COVID-19 pandemic and general economic and market conditions. CPI-0610, CPI-1205 and CPI-0209 are investigational therapies and have not been approved by the FDA (or any other regulatory authority). For a discussion of other risks and uncertainties, any of which could cause the Company's actual results to differ from those contained in the forward-looking statements, see the "Risk Factors" section, as well as discussions of potential risks, uncertainties, and other important factors, in the Company's most recent filings with the Securities and Exchange Commission, including the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2020. In addition, the forward-looking statements included in this press release represent the Company's views as of the date hereof and should not be relied upon as representing the Company's views as of any date subsequent to the date hereof. The Company anticipates that subsequent events and developments will cause the Company's views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, the Company specifically disclaims any obligation to do so.

MANIFEST at EHA

Constellation Pharmaceuticals Analyst/Investor Meeting

Jigar Raythatha

President and CEO

Constellation Pharmaceuticals

Claire Harrison, D.M. (Oxon.)

Professor of Haematology and MANIFEST Investigator

Adrian Senderowicz, M.D.

Chief Medical Officer

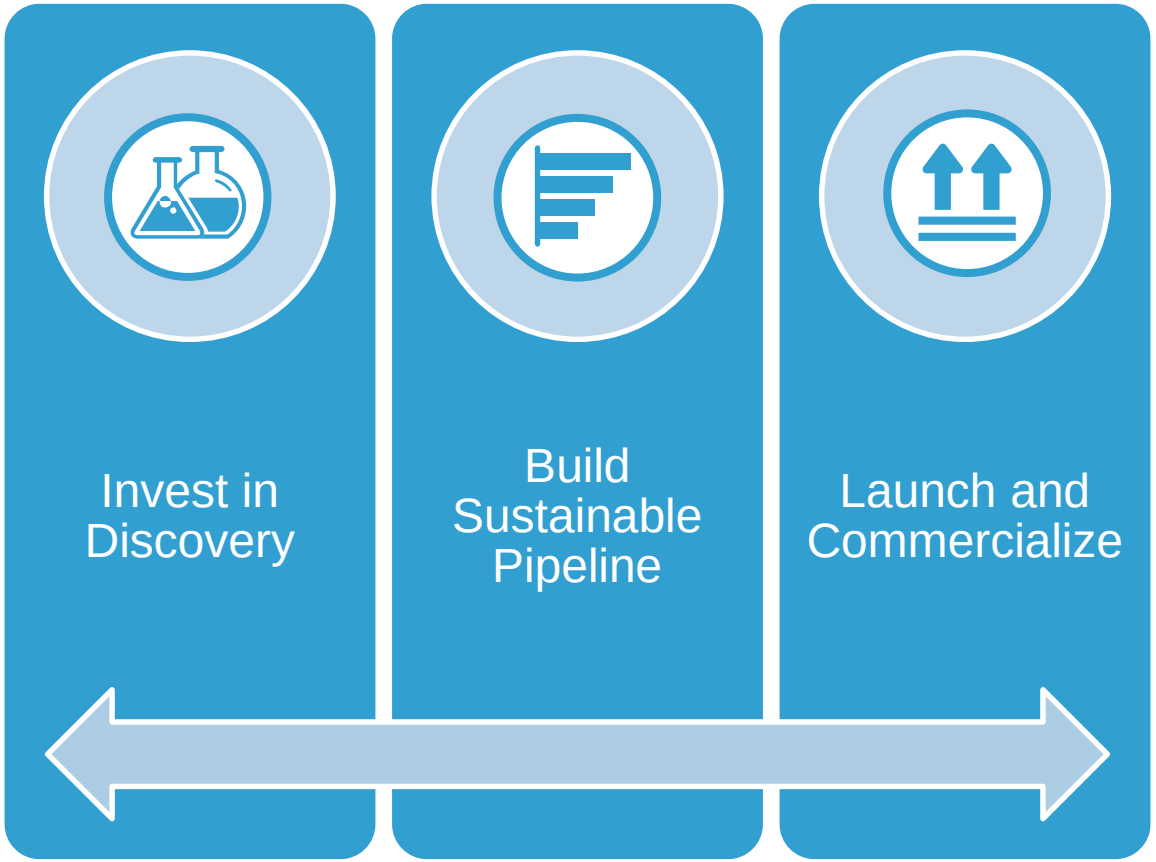
Constellation Pharmaceuticals

Agenda

Topic	Presenter
• ***Company Profile*** • ***Overview of Myelofibrosis (MF)*** • ***Constellation's Vision for CPI-0610***	• ***Jigar Raythatha***
• MANIFEST Clinical Data	• Claire Harrison, D.M. (Oxon.)
• Regulatory Approval Pathway	• Adrian Senderowicz, M.D.
• Commercial Opportunity • Concluding Remarks	• Jigar Raythatha

Constellation Highlights

Building a Fully Integrated Pharmaceutical Company



Goals

- ***Transform Standard of Care for Myelofibrosis*** *with Potential Disease-Modifying Benefits of* ***CPI-0610***
- ***Deliver Best-in-Class EZH2 Therapy*** *and Expand Addressable Patient Population*
- *Create* ***Novel*** *and Impactful Hematology and Oncology* ***Therapies*** *with our* ***Discovery Platform***

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Multiple Near-Term Opportunities for Success

Product Candidates	Indications	Preclinical	Phase 1	Phase 2	Phase 3	Next Steps
BET Inhibitor						
CPI-0610	2L Myelofibrosis 1L Myelofibrosis		**MANIFEST Trial**			• Phase 3 start in 2H20 • MANIFEST update in late 2020
EZH2 Franchise						
CPI-1205	2L mCRPC		**ProSTAR Trial**			• Development of CPI-1205 to be discontinued after ProSTAR
CPI-0209 (2nd Generation)	Solid Tumors					• RP2D in 2H20 • Phase 2 development plan
Preclinical						
Tumor Targeted (Undisclosed)	Solid Tumors/ Heme Malignancies					
Tumor Microenvironment Targeted (Undisclosed)	Solid Tumors					

RP2D = recommended Phase 2 dose mCRPC = metastatic castration-resistant prostate cancer

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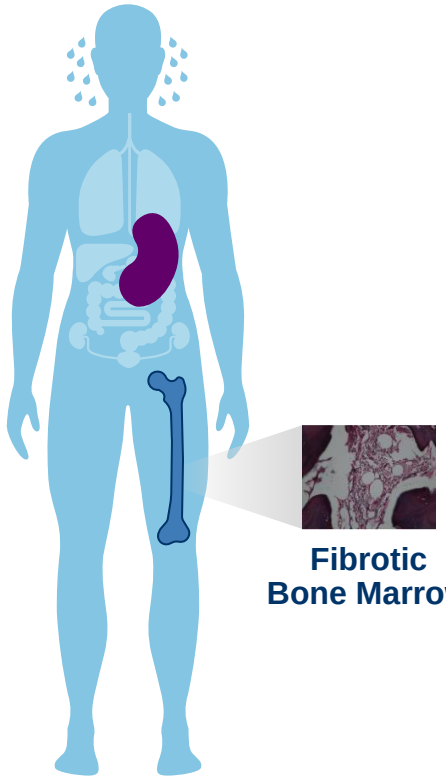
Myelofibrosis Patient Journey

Vision: Transform Standard of Care in MF with a Differentiated Therapeutic Option

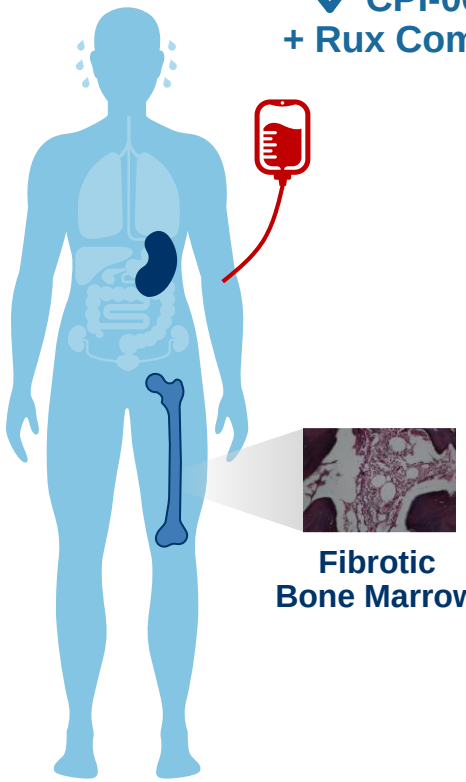
Symptomatic MF



Fibrotic
Bone Marrow

1L: Start JAKi

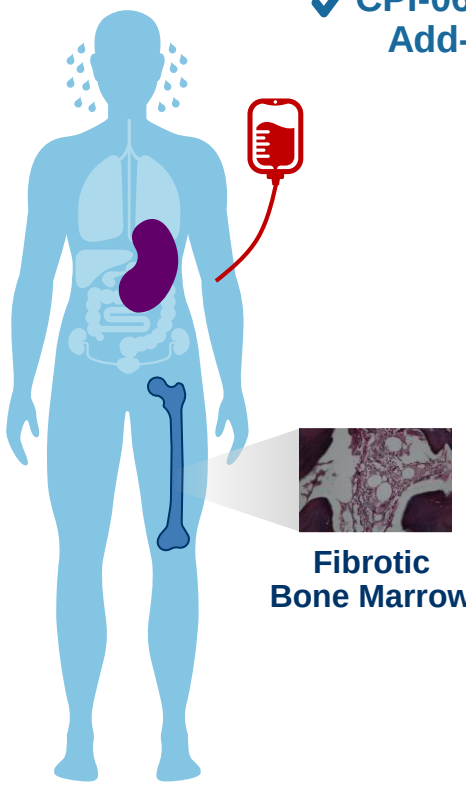
✔ CPI-0610
+ Rux Combo



Fibrotic
Bone Marrow

2L: Continue on JAKi

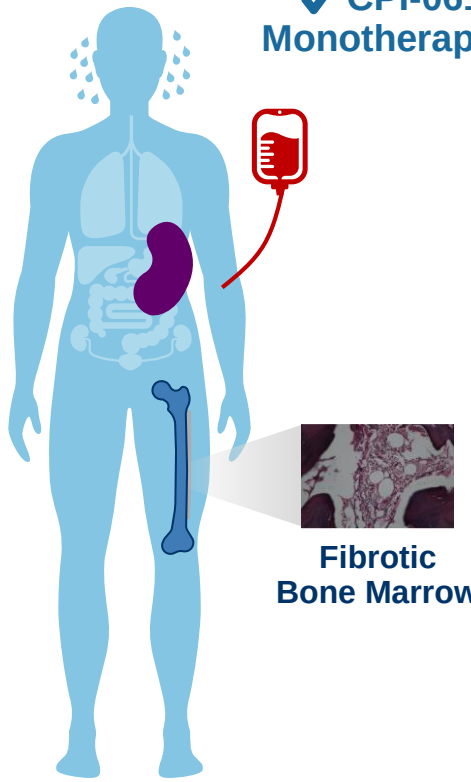
✔ CPI-0610
Add-On



Fibrotic
Bone Marrow

2L: Stop JAKi

✔ CPI-0610
Monotherapy



Fibrotic
Bone Marrow

Disease Progression

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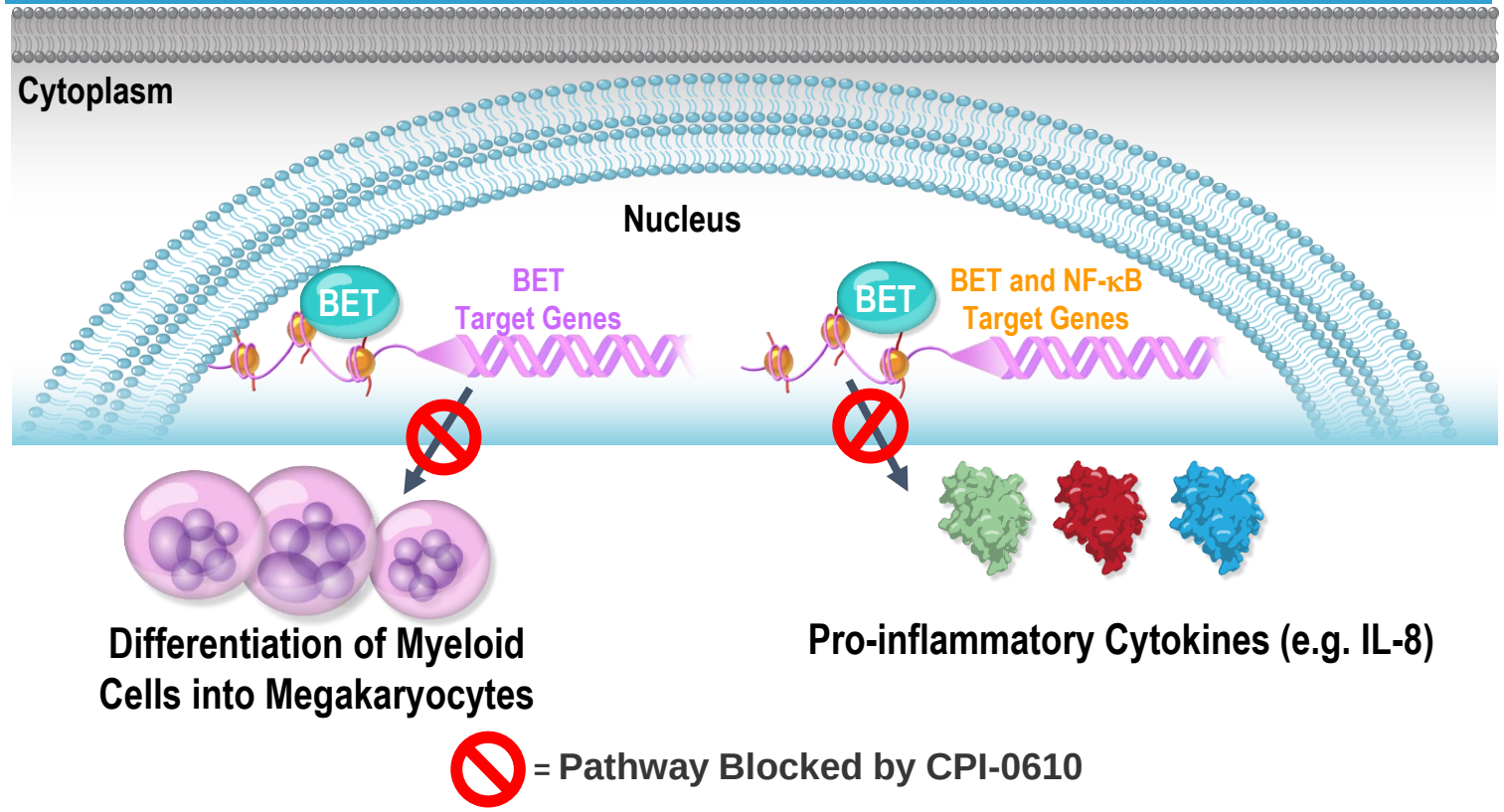
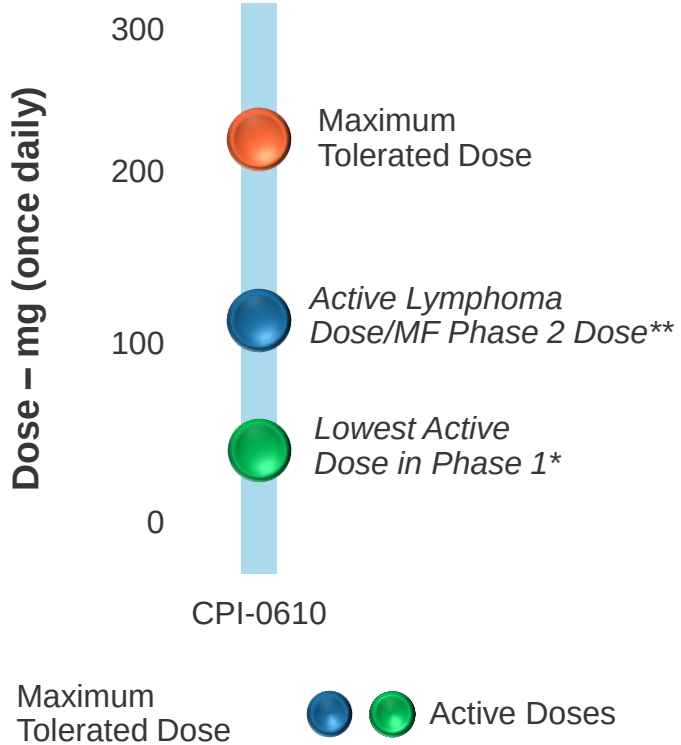
CPI-0610 Is a Potential Best-in-Class BET Inhibitor and Potential Disease-Modifying Therapy for MF

CPI-0610 Mechanism of Action



IL-8 = interleukin-8

Potential for Wide Therapeutic Window with CPI-0610



*CR also achieved at lower dose of 48mg QD capsule
**Ability to titrate up to 225 mg
QD = quaque die (once daily)

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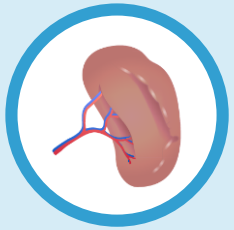
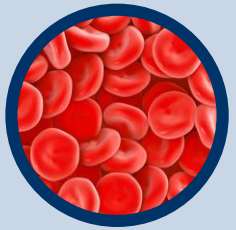
Working to Meet Unmet Needs for a Disease-Modifying Therapy That Impacts All Four Hallmarks of MF

Hallmarks of Myelofibrosis

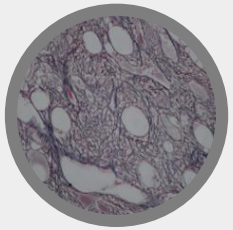


Spleen Volume

Constitutional Symptoms



Anemia & Transfusion Dependence



Bone Marrow Fibrosis

CPI-0610*

* Based on preliminary data as of April 17, 2020

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Summary of MANIFEST Clinical Activity at EHA

Current Benchmarks for Standard of Care in 1L JAKi-Naive

SVR35 Rate	COMFORT-1*	COMFORT-2**	SIMPLIFY-1***
	41.9%	28.5%	29%

SVR35 response = ≥35% spleen volume reduction (Measured at 24 Weeks in COMFORT-1 and SIMPLIFY-1 and at 48 Weeks for COMFORT-2)

* COMFORT-1: A Double-blind, Placebo-controlled Trial of Ruxolitinib for Myelofibrosis. Verstovsek, S., et al; N Engl J Med 2012;366:799-807.

** COMFORT- 2: A Double-blind, Placebo-controlled Trial of Ruxolinib vs. Best Available Therapy (BAT) for Myelofibrosis. Harrison, C., et al; NEJM 2012; 336: 787-798.

*** SIMPLIFY-1: A Phase III Randomized Trial of Momelotinib Versus Ruxolitinib in Janus Kinase Inhibitor-Naïve Patients With Myelofibrosis. Mesa, R., et al. J Clin Oncol 2017: 35(34):3844-3850.

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Consistent High Spleen Volume Response Over Time

JAKi-Naïve Patients in Arm 3 (1L; CPI-0610 + Ruxolitinib)

	ASH 2019	EHA Abstract Update	EHA Poster
12-Week SVR35 Rate	80% (12/15)	72% (21/29)	73% (37/51)

	ASH 2019	EHA Abstract	EHA Poster
24-Week SVR35 Rate	N/A	67% (10/15)	63% (19/30)

Data cut-off for ASH 2019: October 17, 2019
Data cut-off for EHA abstracts: January 9, 2020
Data cut-off for EHA posters: April 17, 2020

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Encouraging Responses in Primary Endpoints in 2L Arms

Active Both as Monotherapy and as Add-on to Ruxolitinib

	Cohort 1A (Monotherapy)	Cohort 2A (Combotherapy)
TD ➔ TI Conversion by 24 Weeks	21% (3/14)	34% (11/32)

	Cohort 1B (Monotherapy)	Cohort 2B (Combotherapy)
24-Week SVR35 Rate	24% (5/21)	22% (4/18)

Data cut-off for EHA presentation: April 17, 2020 Primary endpoint for cohorts 1A and 1B is transfusion dependence to transfusion independence conversion
TD = transfusion dependent: receiving an average of ≥ 2 RBC transfusions per month during the 12 weeks prior to enrollment
TI = transfusion independent, absence of RBC transfusions over any 12 weeks
Primary endpoint for cohorts 1B and 2B is SVR35 at 24 weeks SVR35 response = ≥35% spleen volume reduction from baseline

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Key Takeaways For EHA Update

- CPI-0610 in combination with ruxolitinib or as monotherapy showed preliminary evidence of clinical activity and potential disease-modifying effects
- No evidence of correlation between SVR35 response and baseline risk status, platelet count, or spleen volume
- CPI-0610 as monotherapy and in combination with ruxolitinib was generally well tolerated
- Proceeding to initiate a Phase 3 study in 2H 2020
- CPI-0610 has the potential to transform standard of care in MF

Note: April 17, 2020 data cutoff
SVR35 response = ≥35% spleen volume reduction from baseline

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Agenda

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• Company Profile • Overview of Myelofibrosis (MF) • Constellation's Vision for CPI-0610	• Jigar Raythatha
• ***MANIFEST Clinical Data***	• ***Claire Harrison, D.M. (Oxon.)***
• Regulatory Approval Pathway	• Adrian Senderowicz, M.D.
• Commercial Opportunity • Concluding Remarks	• Jigar Raythatha

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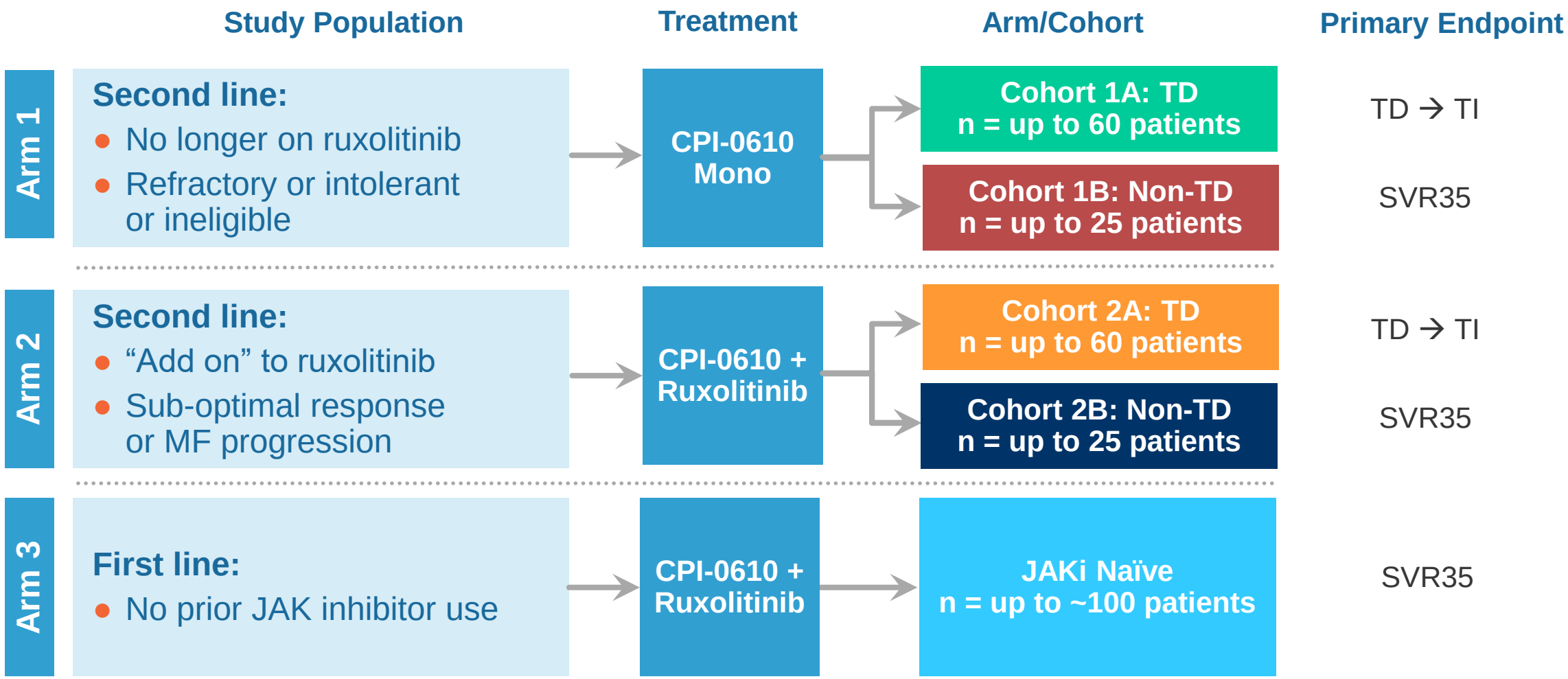
MANIFEST Study Design Overview



TD = transfusion dependent TI = transfusion independent SVR35: ≥35% spleen volume reduction from baseline
TD→TI: TD to TI conversion

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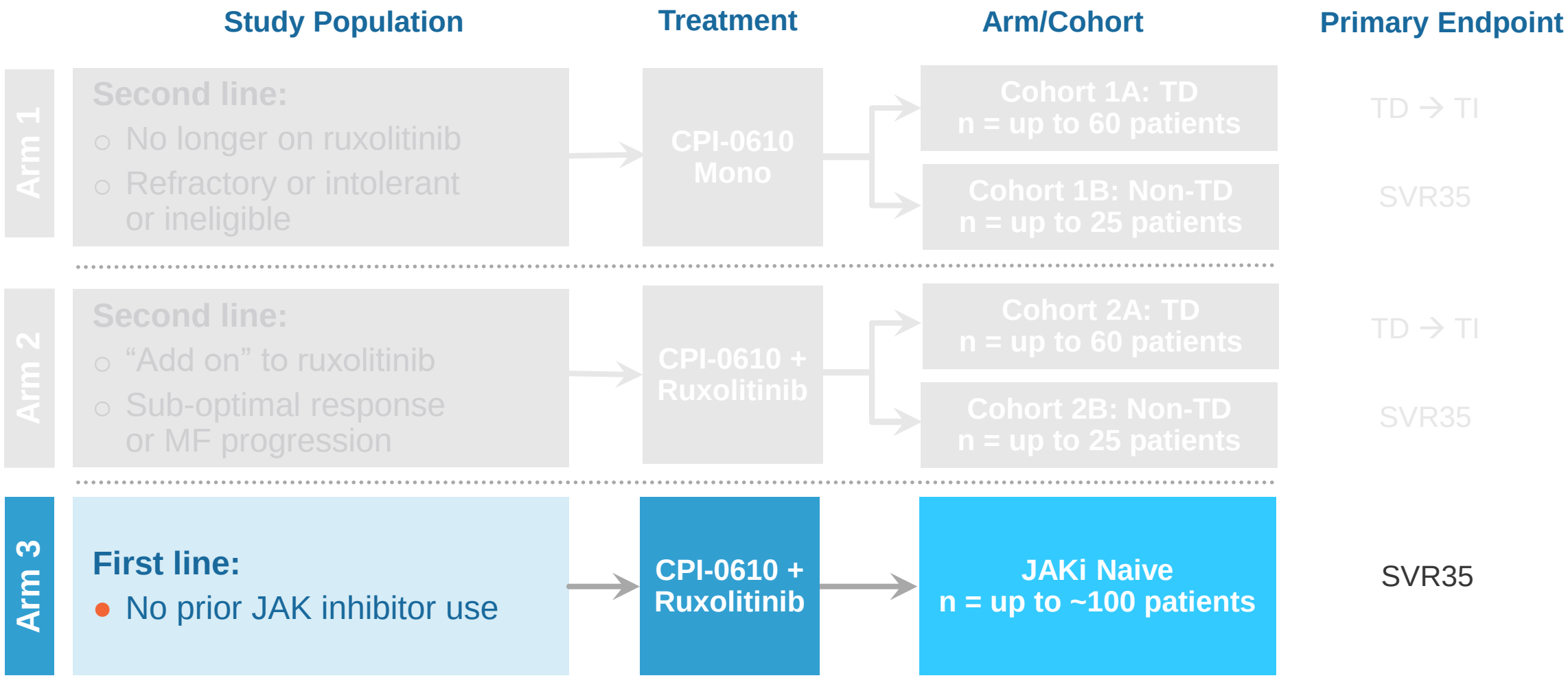
Arm 3: CPI-0610 in Combination with Ruxolitinib in JAK-Inhibitor-Naïve (1L) Patients

April 17, 2020 Data Cutoff

MANIFEST Study Design Overview



SVR35: ≥35% spleen volume reduction from baseline

Arm 3 (JAKi-Naïve Patients): Baseline Demographics and Disease Characteristics

		Safety Population[1] N=64	Primary endpoint evaluable population[2] N=30
Age (years)	Mean (SD)	67.1 (10.27)	65.6 (10.39)
Gender	Male, n (%)	45 (70.3)	22 (73.3)
DIPSS	Int-1, n (%)	16 (25.0)	10 (33.3)
	Int-2, n (%)	40 (62.5)	17 (56.7)
	High, n (%)	8 (12.5)	3 (10.0)
MF Subtype	Primary MF, n (%)	33 (51.6)	15 (50.0)
	Post PV MF, n (%)	6 (9.4)	3 (10.0)
	Post ET MF, n (%)	21 (32.8)	10 (33.3)
Mutations	≥3 mutations, n (%)	41 (64.1)	17 (56.7)
	HMR, n (%)	34 (53.1)	17 (56.7)
	ASXL, n (%)	27 (42.2)	13 (43.3)
	JAKV617F, n (%)	46 (71.9)	20 (66.7)
Hemoglobin (g/dL)	Median (Min, Max)	9.1 (7.0, 16.9)	9.4 (7.3, 13.9)
	<10, n (%)	41 (64.1)	17 (56.7)
Platelet ($x10^9$/L)	Median (Min, Max)	302 (100.0, 1849.0)	350.5 (100.0, 951.0)
Spleen Volume (cc)	Median (Min, Max)	1770.0 (457.0, 4782.0)	1740.5 (457.0, 4782.0)
TSS	Median (Min, Max)	15.5 (0.0, 38.3)	15.6 (4.1, 31.0)

[1]Safety population: All patients who received at least one dose of study drug as of the data cut of April 17, 2020 regardless of length of therapy

[2]Primary endpoint evaluable population: all patients who underwent baseline and week 24 spleen volume assessment or those who discontinued treatment prior to week 24 for any reason

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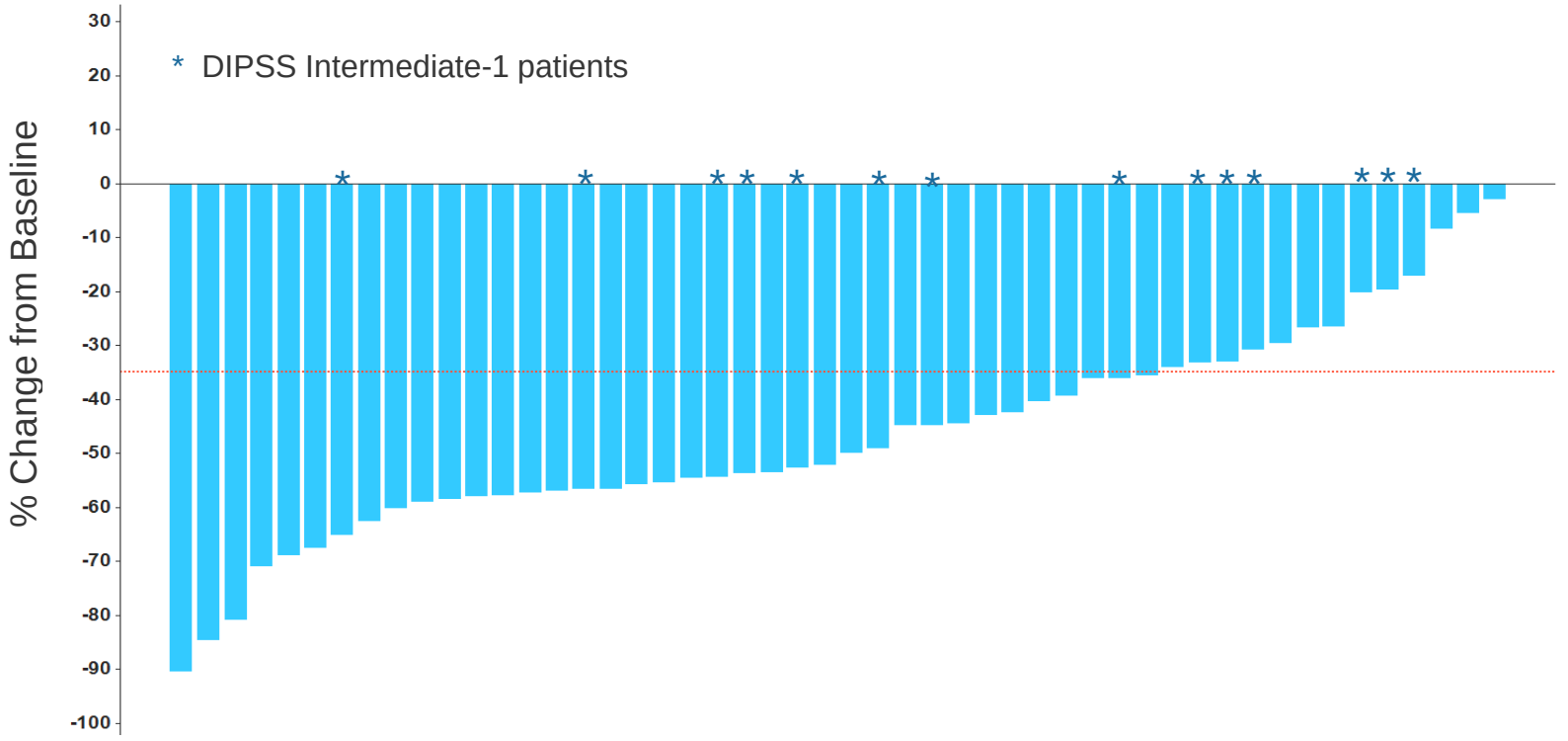
Arm 3 (JAKi-Naïve Patients): Clinically Meaningful Spleen Volume Response at 12 Weeks in a Larger Cohort of Patients

EHA Data:
April 17, 2020 Data Cutoff (n=51)



- 73% (37/51) SVR35 response rate
  - Median % change: –51%
  - Response not driven by *Intermediate-1 patients

Patients are evaluable for SVR35 at week 12 if they have had week 12 spleen volume assessment by the data cutoff date or discontinued prior to week 12 for any reason. SVR35 response = ≥35% spleen volume reduction DIPSS = Dynamic International Prognostic Scoring System Intermediate-1 = 1-2 points for risk factors of: age > 65 years (1 point), constitutional symptoms (1 point), hemoglobin < 10 g/dL (2 points), white blood cell count > 25 x 10^9/L (1 point), circulating blasts ≥ 1% (1 point)

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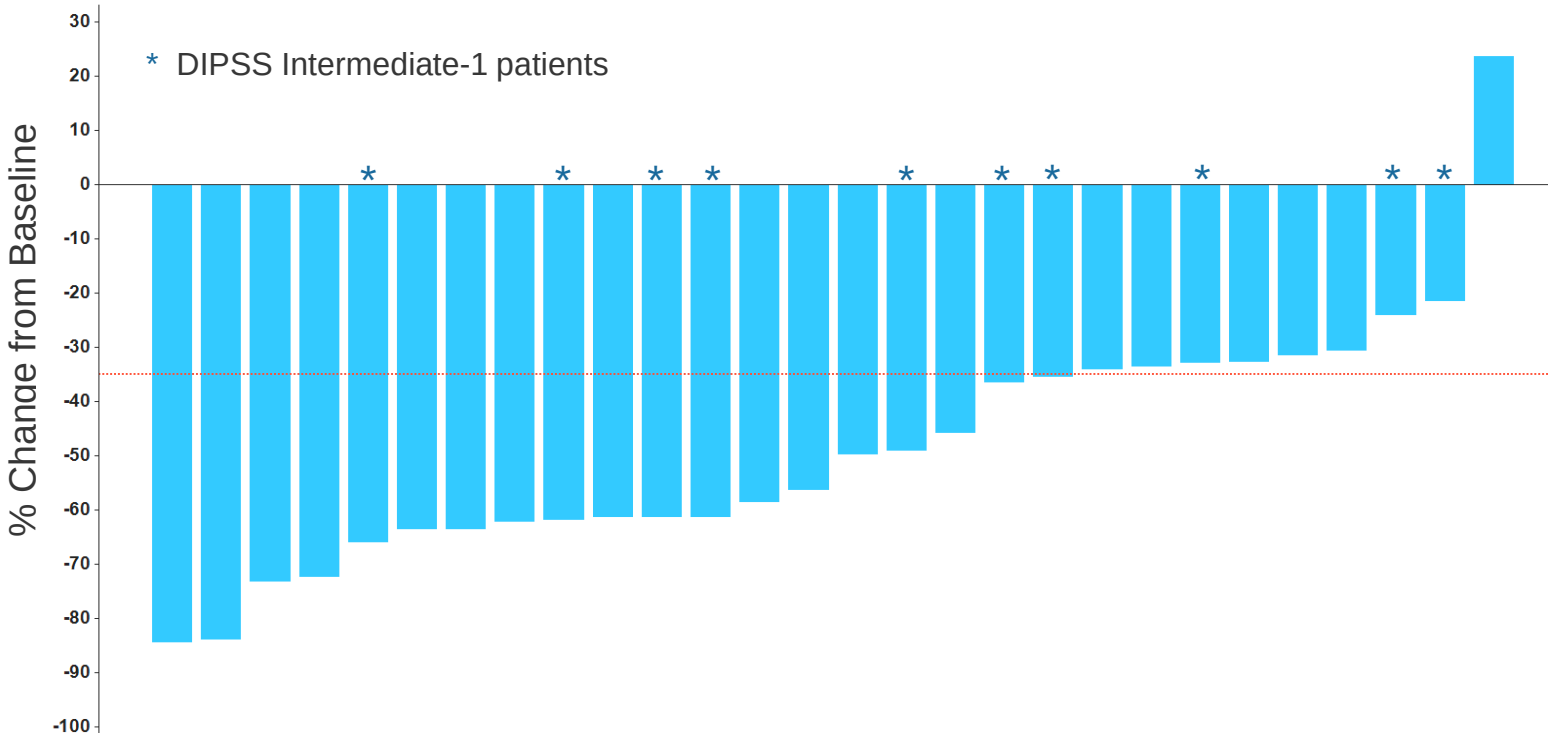
Arm 3 (JAKi-Naïve Patients): Comparable Spleen Volume Response at 24 Weeks

EHA Data:
April 17, 2020 Data Cutoff (n=30)



- 63% (19/30) SVR35 response rate
  - Median % change: -53%
  - Response not driven by *Intermediate-1 patients

Patients are evaluable for SVR35 at week 24 if they have had week 24 spleen volume assessment by the data cutoff date or discontinued prior to week 24 for any reason. Two patients discontinued before 24 weeks.
DIPSS = Dynamic International Prognostic Scoring System Intermediate-1 = 1-2 points for risk factors of: age > 65 years (1 point), constitutional symptoms (1 point), hemoglobin < 10 g/dL (2 points), white blood cell count > 25 x 10^9/L (1 point), circulating blasts ≥ 1% (1 point) SVR35 response = ≥35% spleen volume reduction

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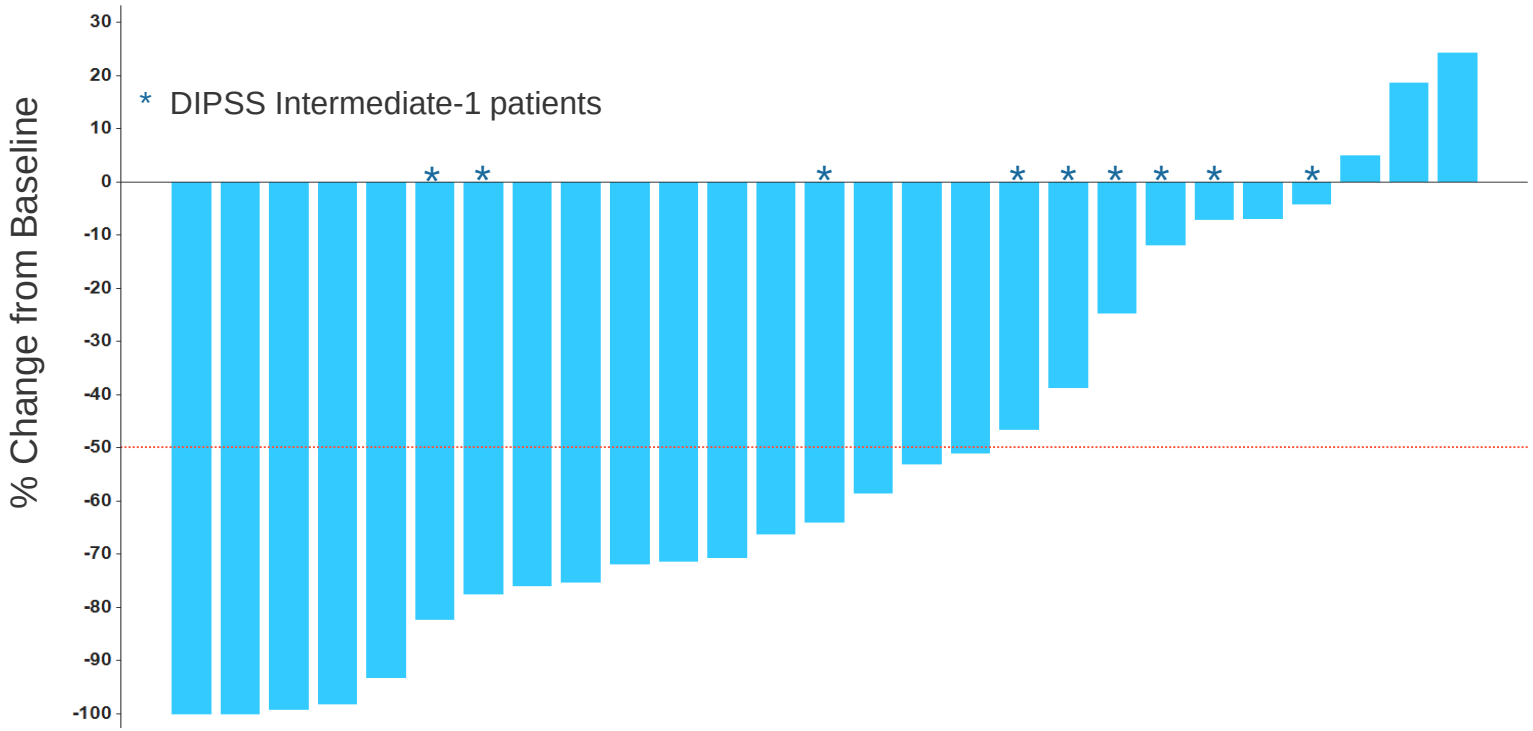
Arm 3 (JAKi-Naïve Patients): Total Symptom Score Change at 24 Weeks

EHA Data:
April 17, 2020 Data Cutoff (n=29)



- 59% (17/29) TSS50 response rate
  - Median % change: -64%
  - Response not driven by *Intermediate-1 patients

Patients are evaluable for TSS50 at week 24 if they have had week 24 spleen volume assessment by the data cutoff date or discontinued prior to week 24 for any reason. One patient was not evaluable due to lacking a baseline measurement for TSS. DIPSS = Dynamic International Prognostic Scoring System Intermediate-1 = 1-2 points for risk factors of: age > 65 years (1 point), constitutional symptoms (1 point), hemoglobin < 10 g/dL (2 points), white blood cell count > 25 x 10^9/L (1 point), circulating blasts ≥ 1% (1 point) TSS50 = ≥50% reduction in Total Symptom Score by Myelofibrosis Symptom Assessment Form version 4.0

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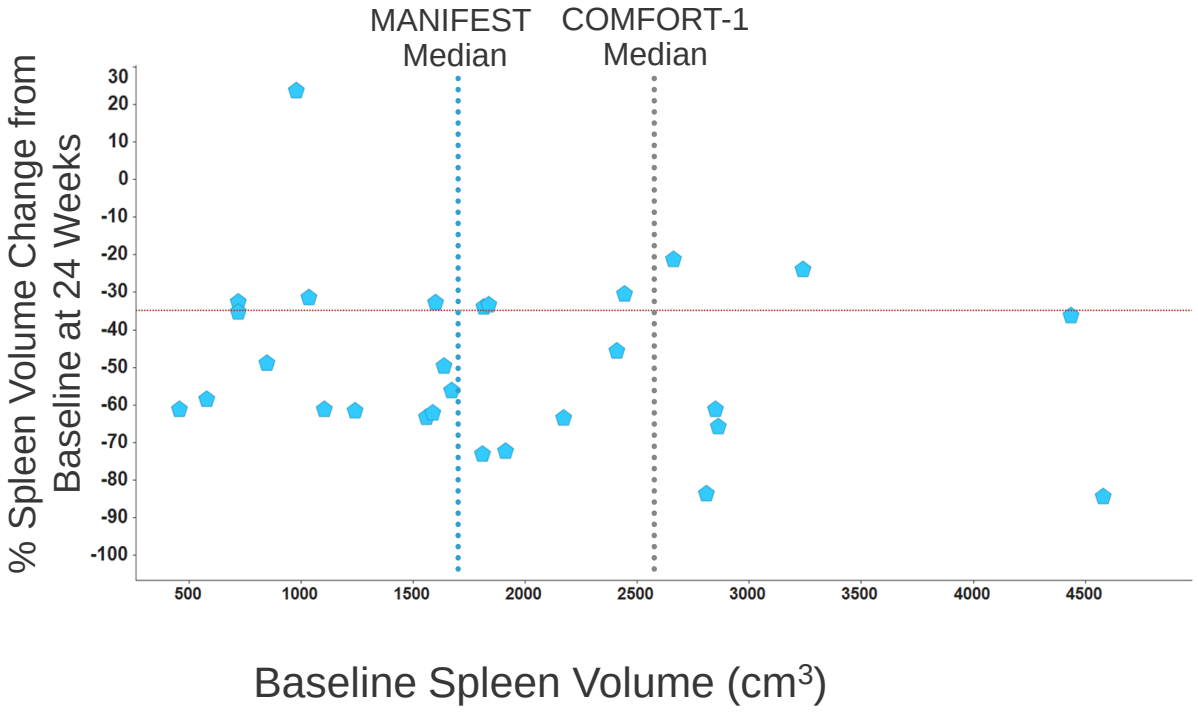
Arm 3 (JAKi-Naïve Patients): SVR35 vs. Baseline Characteristics

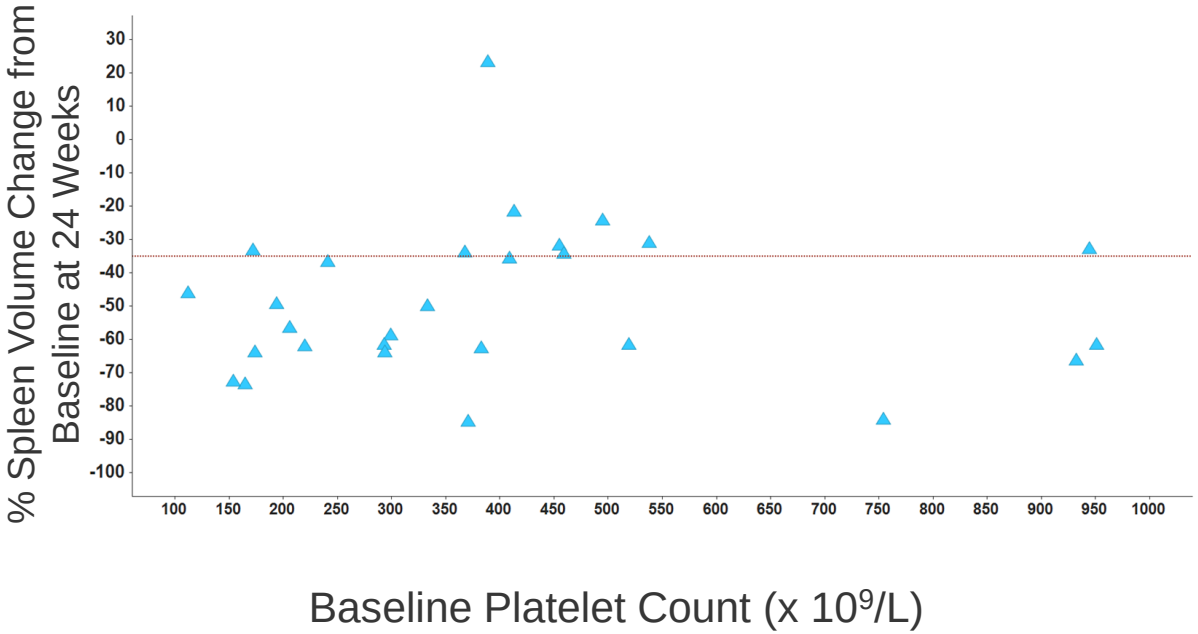
April 17, 2020 Data Cutoff

Spleen Volume Reduction vs. Baseline Spleen Volume



- Suggests a lack of correlation between baseline spleen volume and SVR35

Spleen Volume Reduction vs. Baseline Platelet Count



- Suggests a lack of correlation between baseline platelet count and SVR35

SVR35: ≥35% spleen volume reduction from baseline

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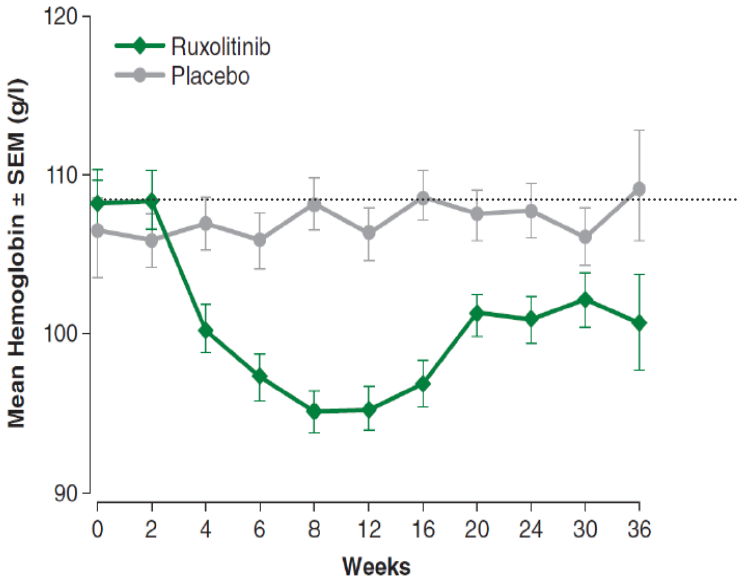
Arm 3 (JAKi-Naïve Patients): Comparative Hemoglobin Changes

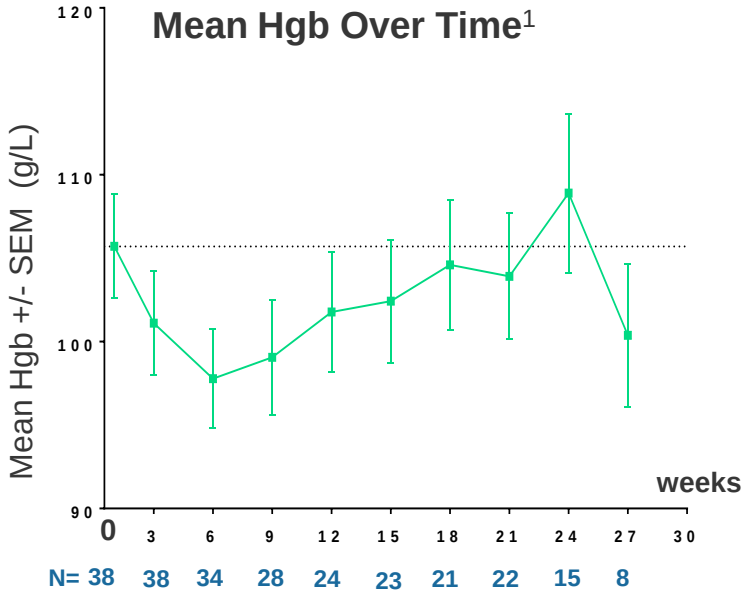
Ruxolitinib in COMFORT-1

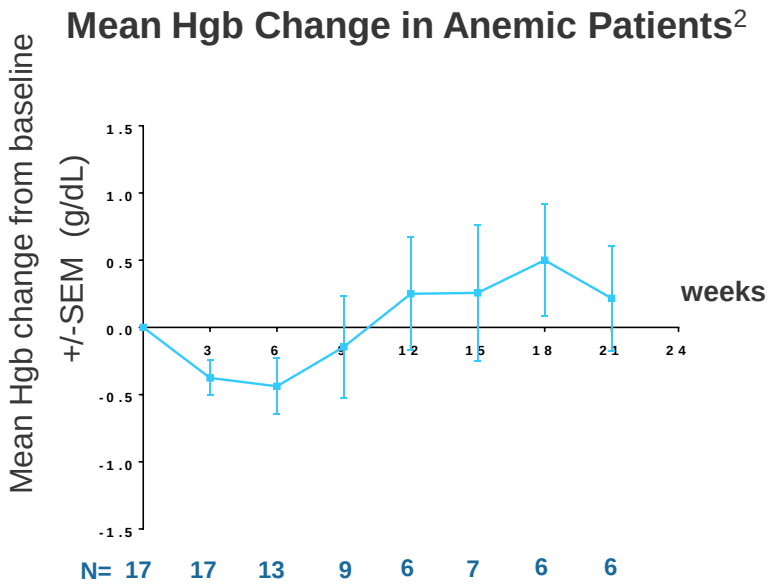


SEM denotes standard error of the mean.

Source: COMFORT-1 publication supplement, Phase 3 trial in 309 myelofibrosis patients

CPI-0610 + Ruxolitinib in MANIFEST Arm 3





[1] Patients on treatment ≥ 12 weeks; hemoglobin values in absence of transfusion within past 12 weeks; timepoints where N>4
[2] Patients with baseline hemoglobin < 10 g/dL
Data cutoff April 17, 2020

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Arm 3: Summary of Safety Profile

CPI-0610 in Combination with Ruxolitinib in 1L Setting Was Generally Well Tolerated

Treatment-Emergent Adverse Events (TEAEs)[1]	All Grade N = 64[2] n (%)	Grade 3 N = 64[2] n (%)	Grade 4 N = 64[2] n (%)
Hematological Events			
Anemia	15 (23.4%)	10 (15.6%)	1 (1.6%)
Thrombocytopenia[3]	13 (20.3%)	1 (1.6%)	2 (3.1%)
Non-Hematological Events			
Gastrointestinal Events			
Diarrhea	17 (26.6%)	0	0
Nausea	12 (18.8%)	0	0
Abdominal Pain	10 (15.6%)	0	0
Other Non-Hematological Events			
Respiratory Tract Infection[4]	12 (18.8%)	2 (3.1%)	1 (1.6%)
Dysgeusia	9 (14.1%)	0	0
Fatigue	8 (12.5%)	0	0
Headache	7 (10.9%)	0	0
Back Pain	7 (10.9%)	0	0

- None of the hematological TEAEs were serious adverse events (SAEs)
- The most common non-hematologic TEAEs were primarily Grade 1/2 – diarrhea, nausea, respiratory tract infection, and abdominal pain
- Four patients discontinued study treatment due to AEs
  - Three cases of infection and one case of Grade 4 thrombocytopenia
- Two AEs were Grade 5, both from multi-organ failure due to sepsis

[1] TEAEs of all grade that occurred in ≥10% of patients; data as of cutoff date of April 17, 2020
[2] Safety evaluable population: Received at least one dose of study drug at the time of the data cut
[3] Includes TEAE platelet count decrease
[4] Includes TEAEs of upper respiratory tract infection, influenza, bronchitis, sinusitis, rhinitis, nasopharyngitis, pneumonia, and pulmonary sepsis

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MANIFEST Arm 3 (JAKi-Naïve Patients): Key Takeaways

April 17, 2020 Data Cutoff

- CPI-0610 in combination with ruxolitinib demonstrated preliminary evidence of compelling activity in 1L MF
- SVR35 rates in 1L patients at 12 weeks and 24 weeks were in line with previously reported data and differentiated from standard of care
- No evidence of correlation was seen between SVR35 response and baseline risk status, platelet count, or spleen volume
- CPI-0610 in combination with ruxolitinib was generally well tolerated
- CPI-0610 has potential to be disease-modifying therapy and to redefine standard of MF care

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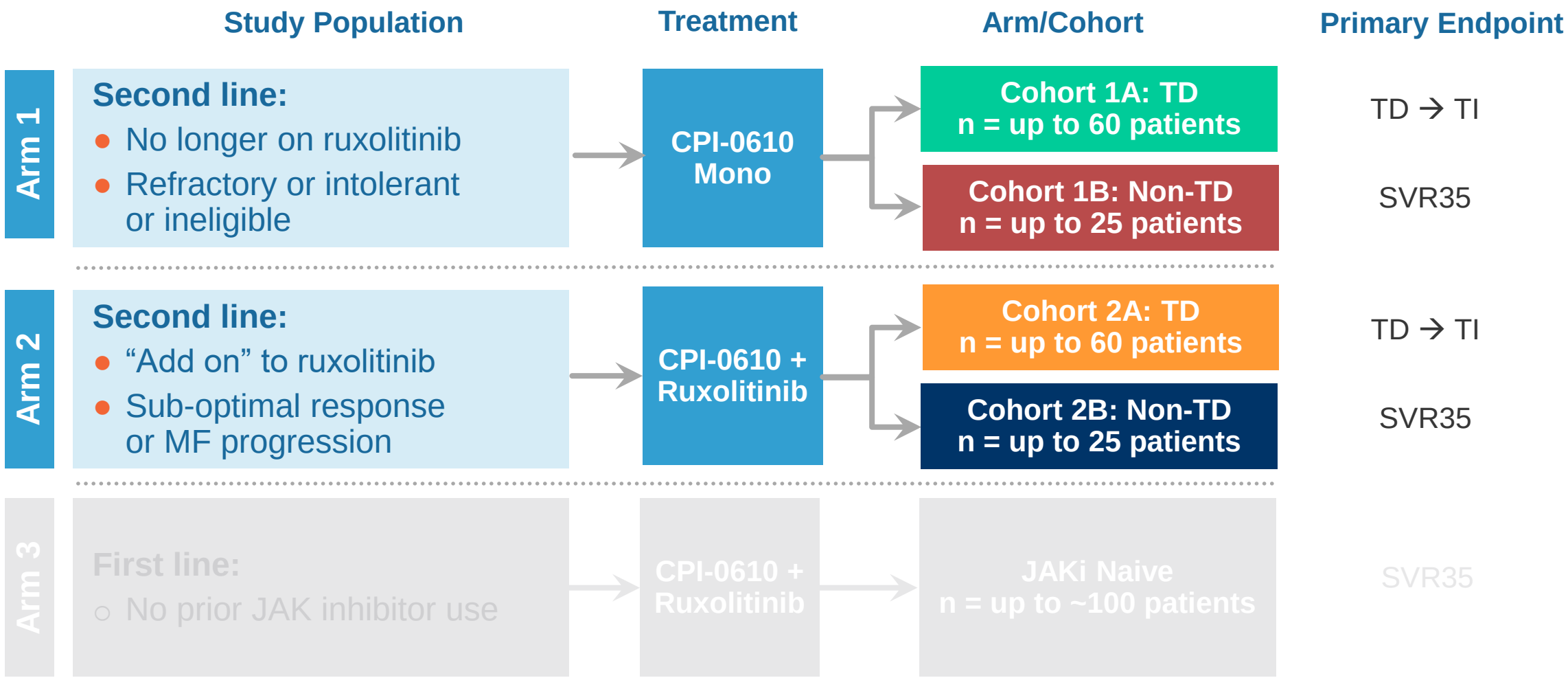
Arm 1 and 2: CPI-0610 as Monotherapy or in Combination With Ruxolitinib in JAKi-Refractory, -Intolerant or -Ineligible (2L) Patients

April 17, 2020 Data Cutoff

MANIFEST Study Design Overview



TD = transfusion dependent: receiving an average of ≥ 2 RBC transfusions per month during the 12 weeks prior to enrollment
TI = transfusion independent, absence of RBC transfusions over any 12 weeks
TD→TI: TD to TI conversion
SVR35: ≥35% spleen volume reduction from baseline

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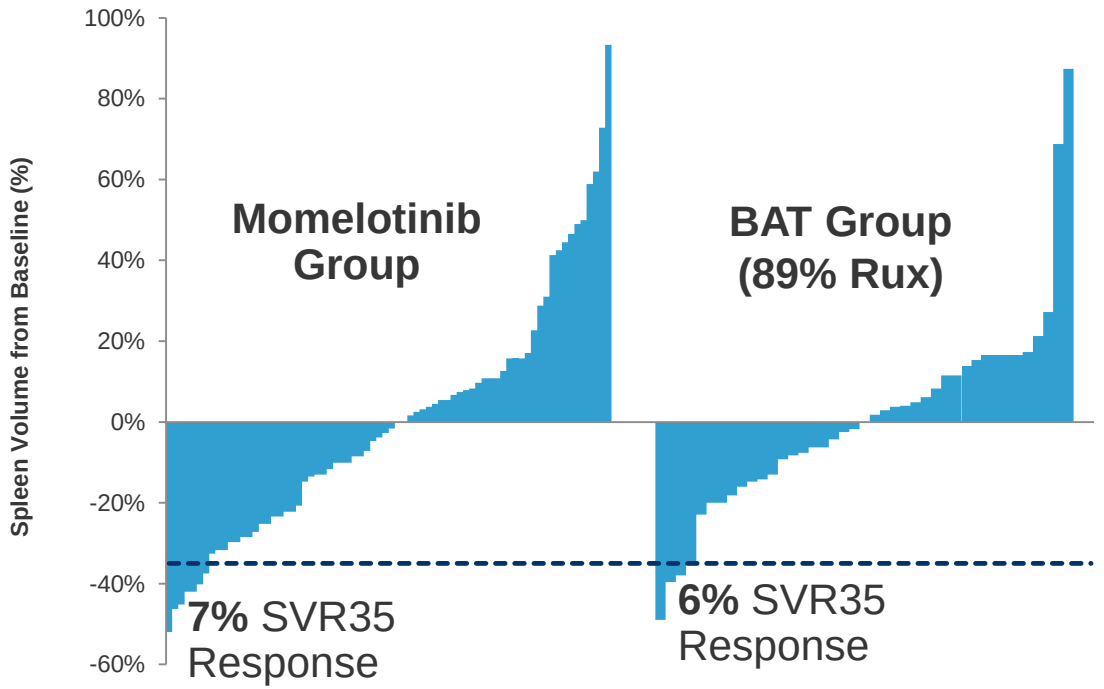
Low Historical Spleen Volume Response Rates in 2L MF

SVR35 Response Rates of JAK Inhibitors in SIMPLIFY-2



- Half of 2L patients on JAK inhibitors in SIMPLIFY-2 experienced spleen volume increases
- Few JAK-inhibitor patients in SIMPLIFY-2 achieved SVR35 responses

Source: CN Harrison et al., Momelotinib versus best available therapy in patients with myelofibrosis previously treated with ruxolitinib (SIMPLIFY 2): a randomised, open-label, phase 3 trial, Lancet Haematology, Volume 5, Issue 2, February 2018, Pages e73-e81.

SVR35 response = ≥35% spleen volume reduction

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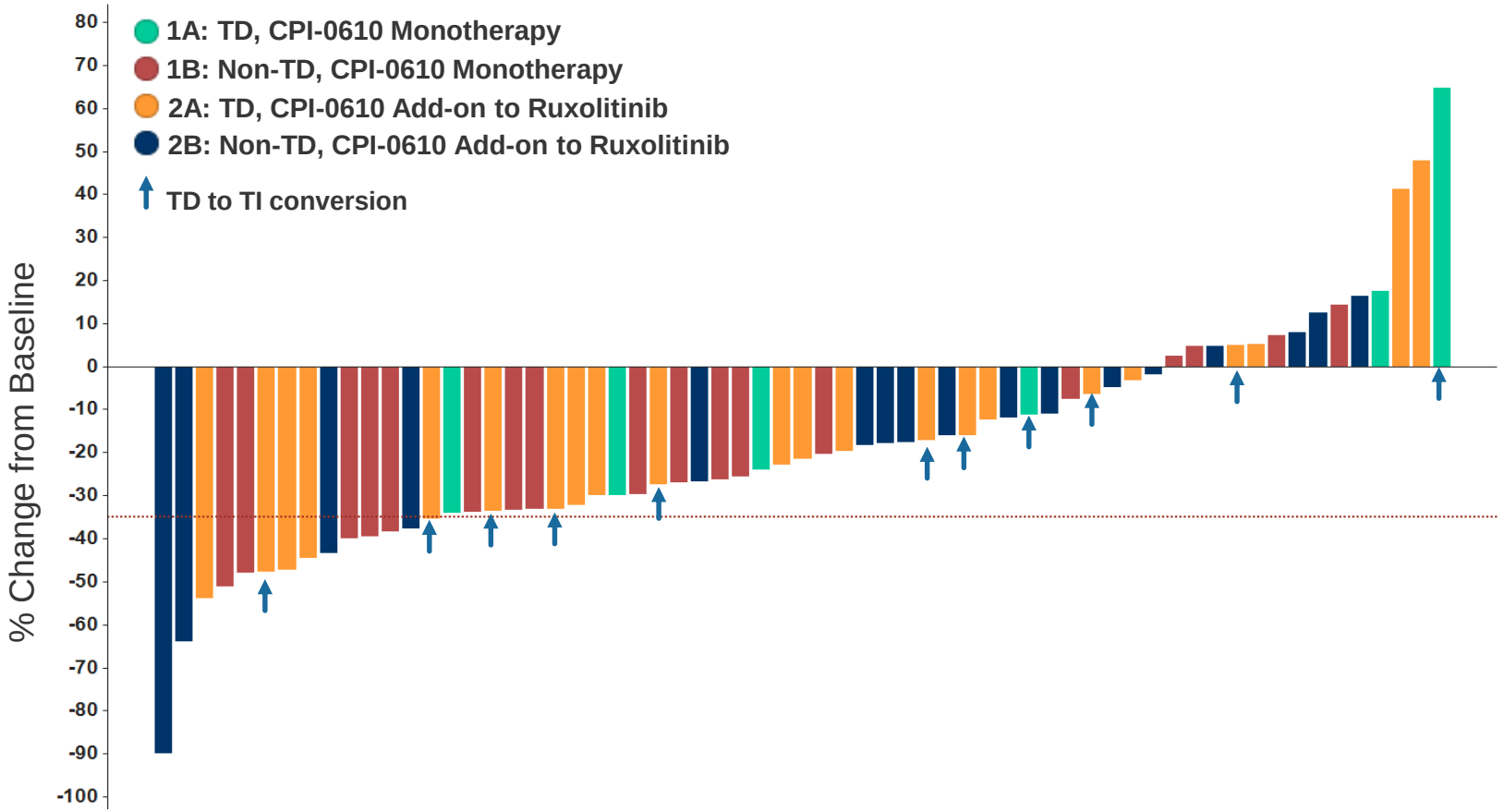
Arms 1 and 2: Spleen Volume Change in 2L Patients at 24 Weeks

April 17, 2020 Data Cutoff



Arm 1 Primary Endpoints

- 1A: TD to TI conversion: 21.4% (3/14)
- 1B: SVR35: 23.8% (5/21)

Arm 2 Primary Endpoints

- 2A: TD to TI conversion: 34.4% (11/32)
- 2B: SVR35: 22.2% (4/18)

Patients are evaluable for transfusion dependent (TD) to transfusion independent (TI) conversion if they have been on treatment for at least 24 weeks by the data cutoff date or if they have been on treatment for at least 12 weeks by the data cutoff day and have achieved the conversion or would have failed to achieve the conversion by week 24. Patients are evaluable for SVR35 at week 24 if they have had week 24 assessment by the data cutoff date or discontinued after having had a week 12 assessment.
SVR35 response = ≥35% spleen volume reduction TD: transfusion dependent, receiving an average of ≥ 2 RBC transfusions per month during the 12 weeks prior to enrollment TI: transfusion independent, absence of RBC transfusions over any 12 weeks

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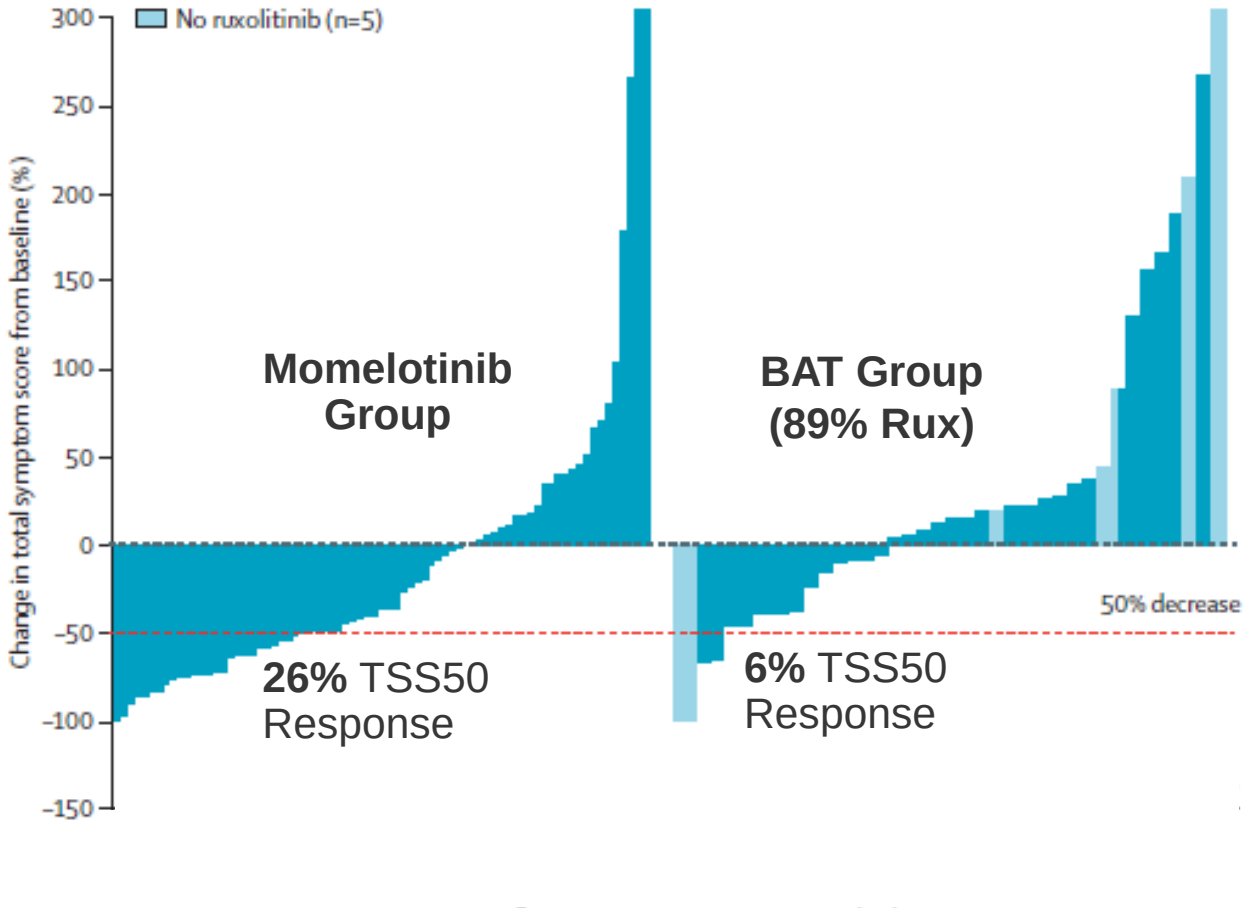
Low Historical TSS50 Response Rates in 2L MF

TSS50 Response Rates of JAK Inhibitors in SIMPLIFY-2



- About two thirds of momelotinib patients achieved overall symptom improvement and about one quarter achieved TSS50
- About one third of BAT (primarily ruxolitinib) patients achieved overall symptom improvement and few achieved TSS50

Source: CN Harrison et al., Momelotinib versus best available therapy in patients with myelofibrosis previously treated with ruxolitinib (SIMPLIFY 2): a randomised, open-label, phase 3 trial, Lancet Haematology, Volume 5, Issue 2, February 2018, Pages e73-e81.

TSS50 response = ≥50% Total Symptom Score improvement BAT = best available therapy

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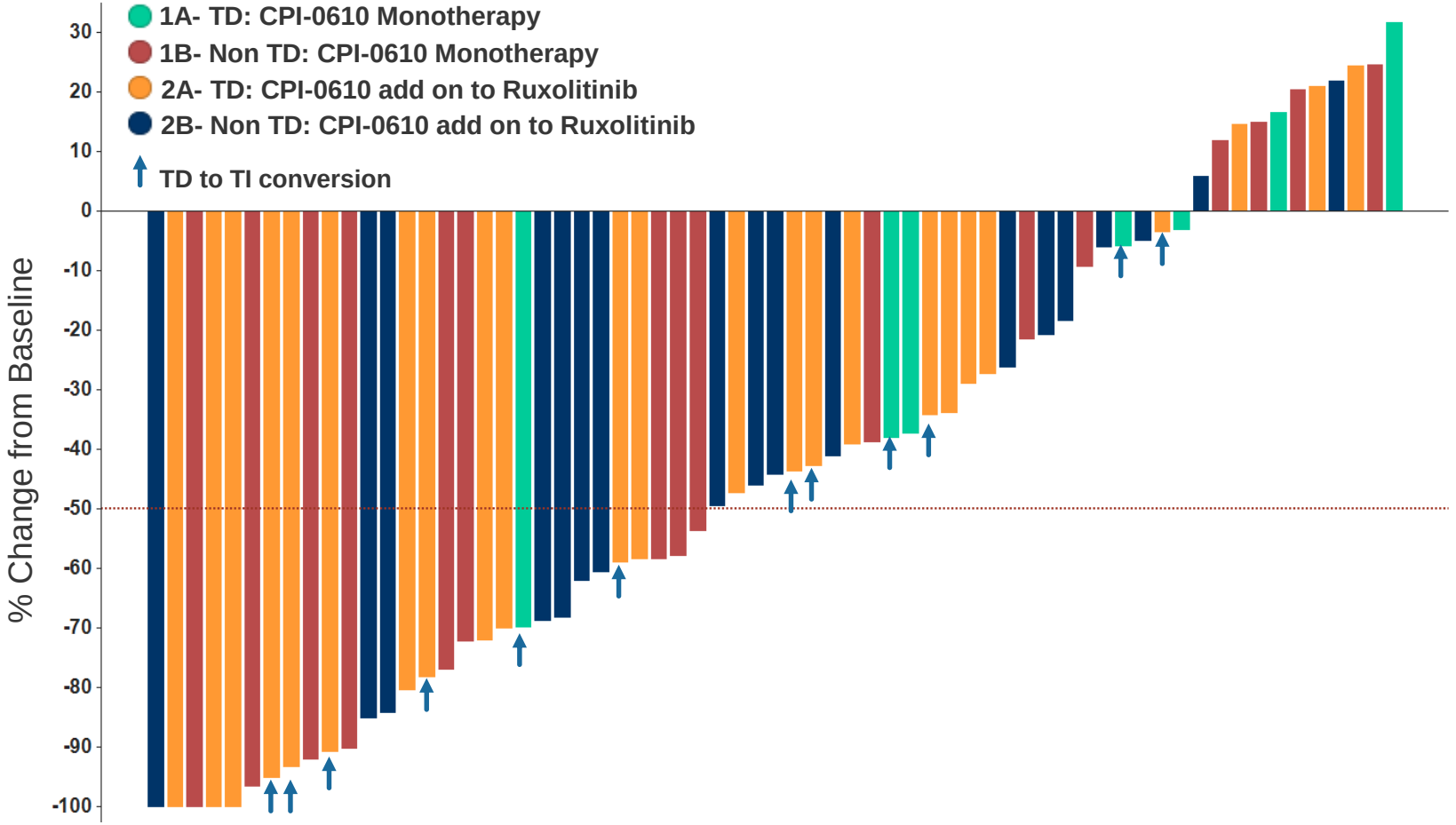
Arms 1 and 2: Total Symptom Score Change in 2L Patients at 24 Weeks

April 17, 2020 Data Cutoff



Arm 1 Secondary Endpoint

- 1A: TSS50: 8.3% (1/12)
- 1B: TSS50: 47.4% (9/19)

Arm 2 Secondary Endpoint

- 2A: TSS50: 46.2% (12/26)
- 2B: TSS50: 36.8% (7/19)

Patients are evaluable for transfusion dependent (TD) to transfusion independent (TI) conversion if they have been on treatment for at least 24 weeks by the data cutoff date or if they have been on treatment for at least 12 weeks by the data cutoff day and have achieved the conversion or would have failed to achieve the conversion by week 24.
Patients are evaluable for TSS50 at week 24 if they have had a week 24 assessment by the data cutoff date or discontinued after having had a week 12 assessment.
TD: Receiving an average of ≥ 2 RBC transfusions per month during the 12 weeks prior to enrollment; TI: Absence of RBC transfusions over any 12 weeks
TSS50 response = ≥50% Total Symptom Score improvement

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Arms 1 and 2: Summary of Safety Profile

CPI-0610 as Monotherapy and in Combo with Ruxolitinib in 2L Setting Was Generally Well Tolerated

Treatment-Emergent Adverse Events[1]	Arm 1			Arm 2		
	All Grade N = 43[2] n (%)	Grade 3 N = 43[2] n (%)	Grade 4 N = 43[2] n (%)	All Grade N = 70[2] n (%)	Grade 3 N = 70[2] n (%)	Grade 4 N = 70[2] n (%)
Hematological Events						
Thrombocytopenia[3]	11 (25.6%)	6 (14.0%)	0	33 (47.1%)	16 (22.9%)	1 (1.4%)
Anemia[4]	5 (11.6%)	4 (9.3%)	0	8 (11.4%)	5 (7.1%)	1 (1.4%)
Non-Hematological Events						
Gastrointestinal Events						
Nausea	14 (32.6%)	0	0	25 (35.7%)	2 (2.9%)	0
Diarrhea	13 (30.2%)	2 (4.7%)	0	36 (51.4%)	3 (4.3%)	0
Abdominal Pain				14 (20.0%)	1 (1.4%)	0
Other Non-Hematological Events						
Respiratory Tract Infection[5]	12 (27.9%)	1 (2.3%)	0	25 (35.7%)	3 (4.3%)	0
Dysgeusia	12 (27.9%)	0	0	15 (21.4%)	0	0
Cough	12 (27.9%)	0	0	17 (24.3%)	0	0
Fatigue	9 (20.9%)	0	0	16 (22.9%)	4 (5.7%)	0

- TEAEs led to study drug discontinuation in six patients in Arm 1 and seven patients in Arm 2
- There were four deaths reported in Arm 2
  - Acute kidney injury
  - Traumatic subdural hematoma (mechanical fall)
  - Brain stem hemorrhage (no concomitant thrombocytopenia)
  - Disease progression

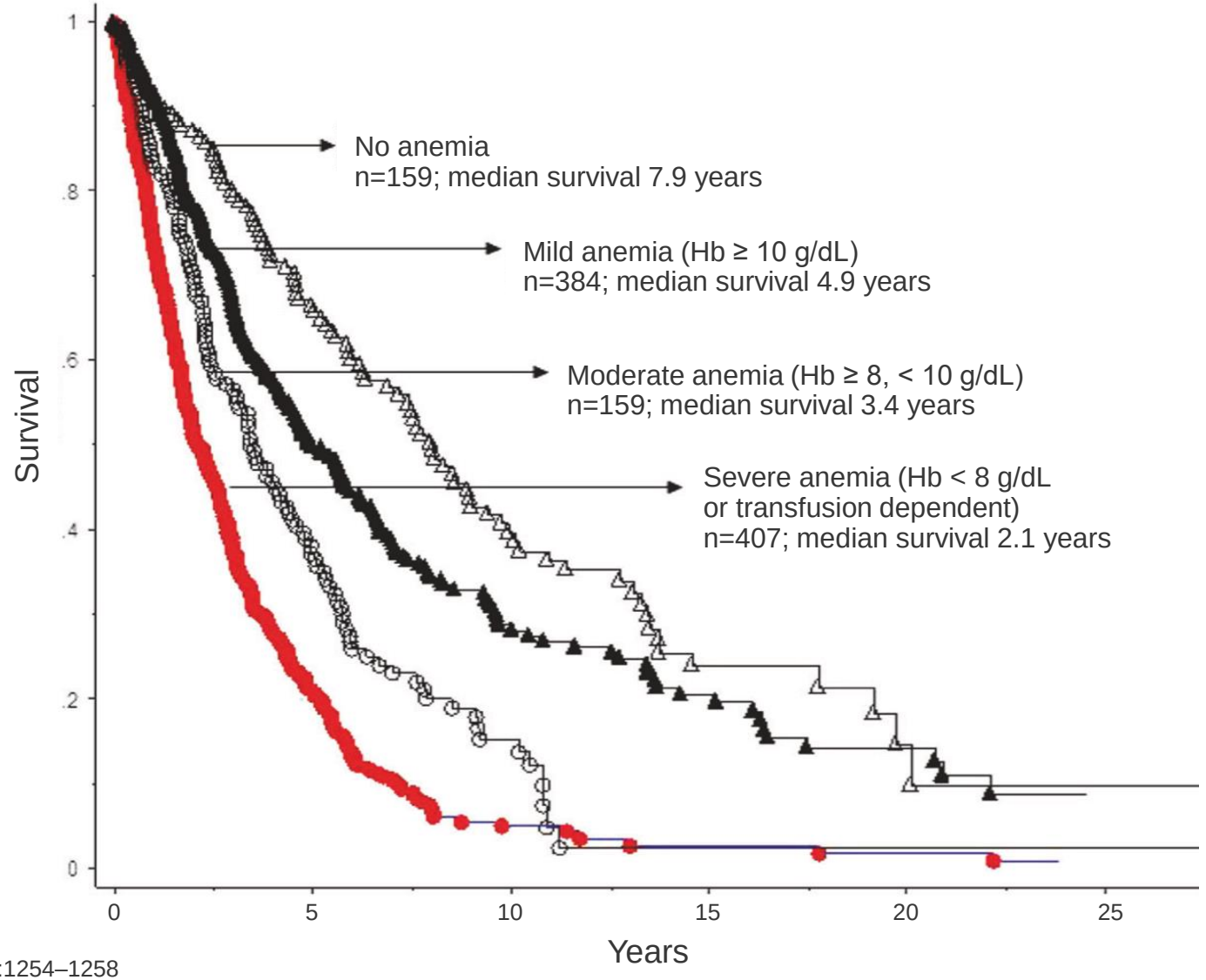
[1] TEAEs of all grade that occurred in ≥20% of patients. [2] Safety evaluable population: Received at least one dose of study drug as of the data cut. [3] Includes TEAE platelet count decrease. [4] TEAE of special interest although occurred in <20% of pts. [5] Includes TEAEs of upper respiratory tract infection, viral upper respiratory tract infection, lower respiratory tract infection, influenza, laryngitis, parainfluenza virus infection, bronchitis, sinusitis, rhinitis, rhinovirus infection, nasopharyngitis, pneumonia
Data cutoff of April 17, 2020

MANIFEST Arms 1 and 2: Key Takeaways

April 17, 2020 Data Cutoff

- Preliminary evidence of compelling activity of CPI-0610 monotherapy seen to date in 2L MF setting
- Promising transfusion independence conversion rate (primary endpoint for TD cohorts)
- SVR35 reductions observed in difficult 2L setting (primary endpoint for non-TD cohorts)
- Generally well tolerated as a monotherapy and in combination with ruxolitinib
- Preliminary data show hemoglobin improvement in CPI-0610 monotherapy

Anemia: Important Prognostic Factor in MF

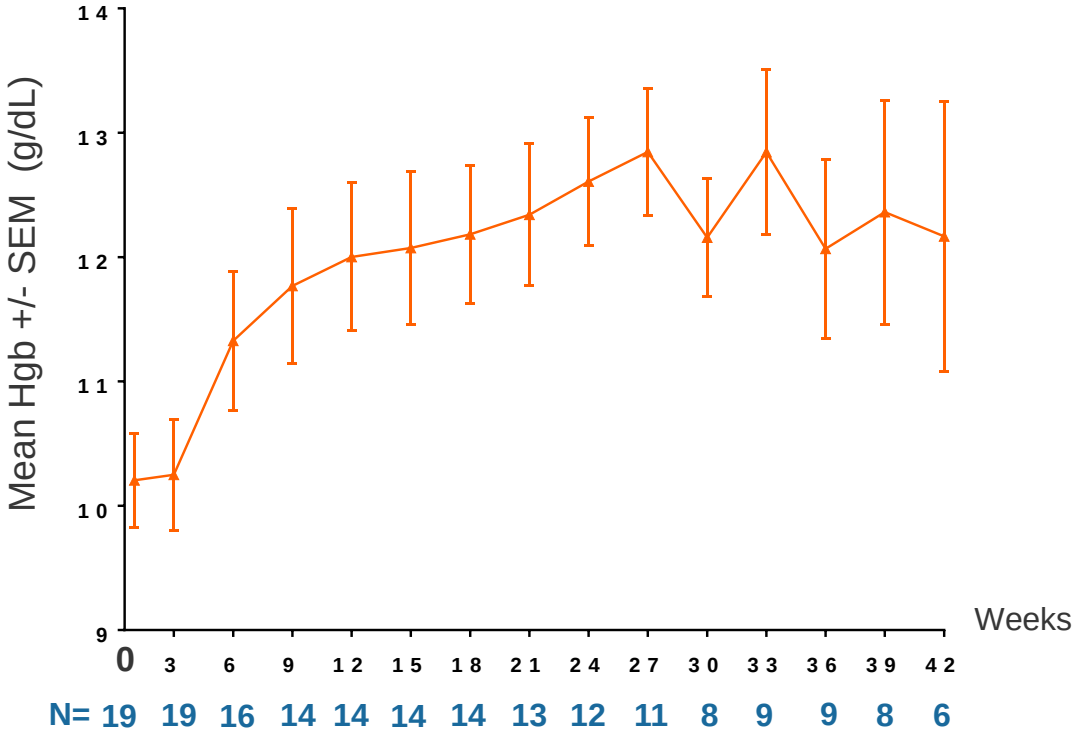


Nicolosi et al. Leukemia 2018 32:1254–1258

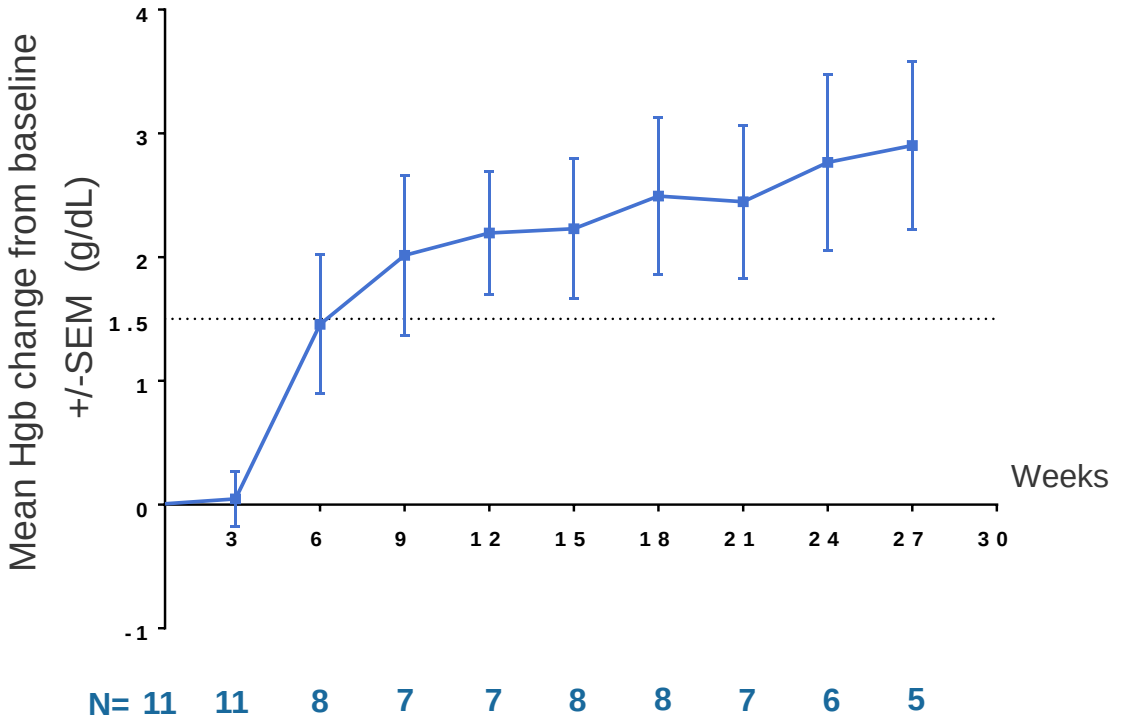
Arm 1B: CPI-0610 Provided Hemoglobin Benefit as Monotherapy

Mean Hemoglobin Over Time[1]

- **57.9% (11/19) patients had ≥1.5 g/dL increase in hemoglobin[2]**



Mean Hemoglobin Change from Baseline[1] for Anemic[3] Patients



[1] Patients on treatment ≥12 weeks; hemoglobin values in absence of transfusion within past 12 weeks; timepoints where n >4
[2] The 1.5 g/dL hemoglobin change from baseline without any transfusion within past 12 weeks
[3] Patients with baseline hemoglobin <10g/dL
Data cutoff April 17, 2020

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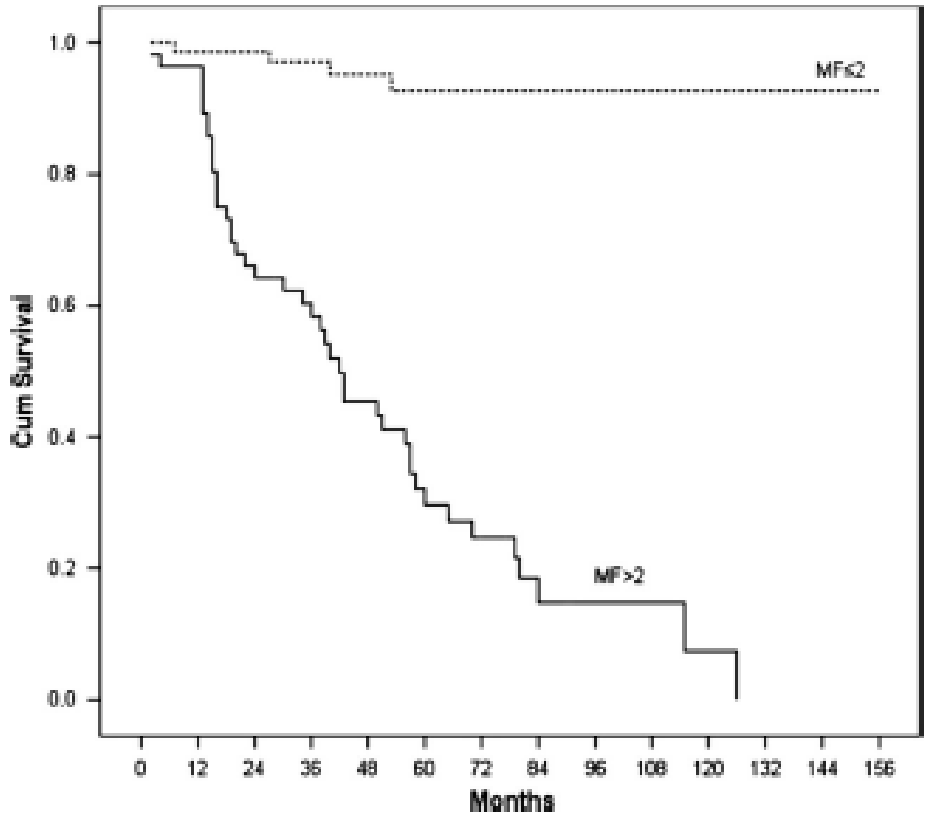
Bone Marrow Fibrosis Is Associated with Poor Prognosis



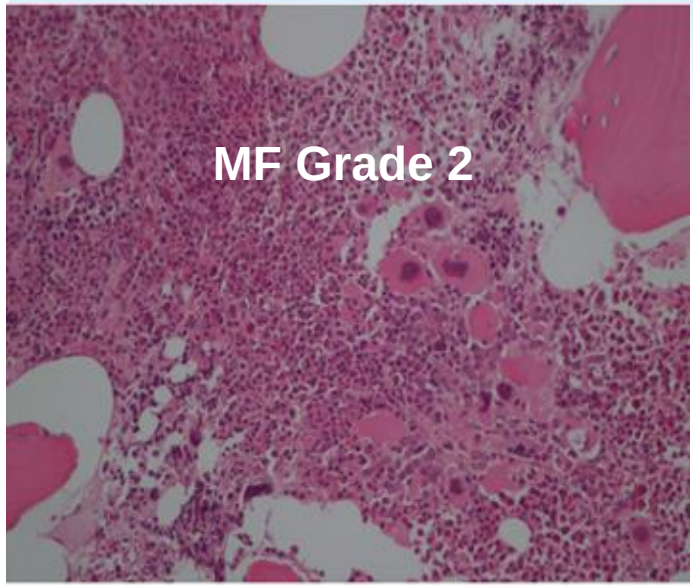
Kaplan–Meier estimate of survival according to the MF $\leq$ 1 versus MF $>$ 1 ($P < 0.001$)

Lekovic et al. Med Oncol (2014) 31:869

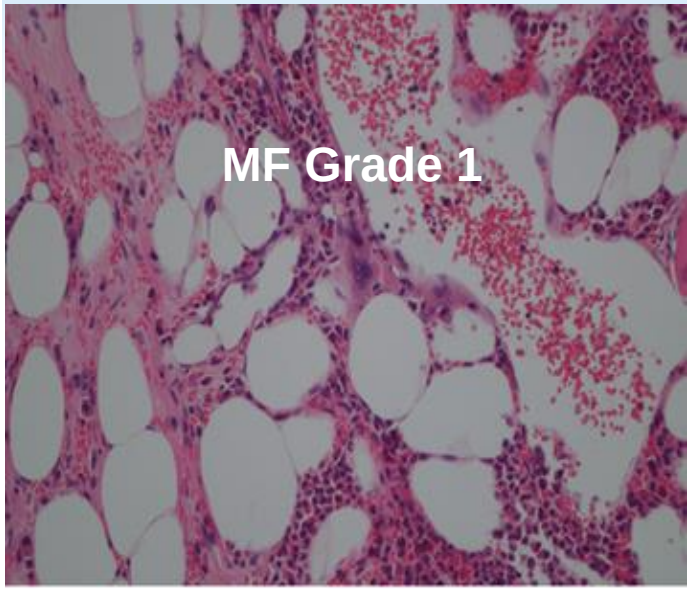
Example of Bone Marrow Fibrosis Improvement

Heavily Pre-Treated Patient With *ASXL1* and *JAK2* Mutation

Baseline



Cycle 17



- Central lab evaluations are planned to confirm bone marrow fibrosis score
- Results to be presented in a translational publication in 2020

ASXL1 = additional sex combs like 1 *JAK2* = Janus kinase 2

Data assessed by local labs per the European consensus on grading bone marrow fibrosis and assessment of cellularity (Thiele J et al. *Haematologica.* 2005;90:1128)

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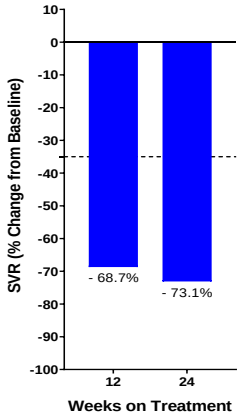
Patient Case Study: Arm 3

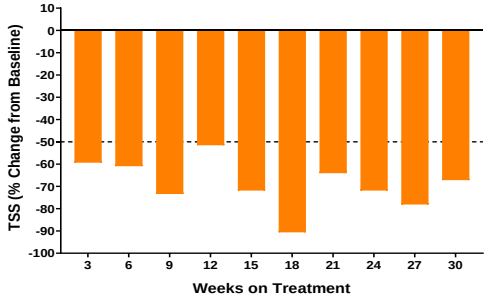
CPI-0610 Has Potential to Impact Hallmarks of MF

Spleen and Symptom Impact

✓ **Spleen Volume**



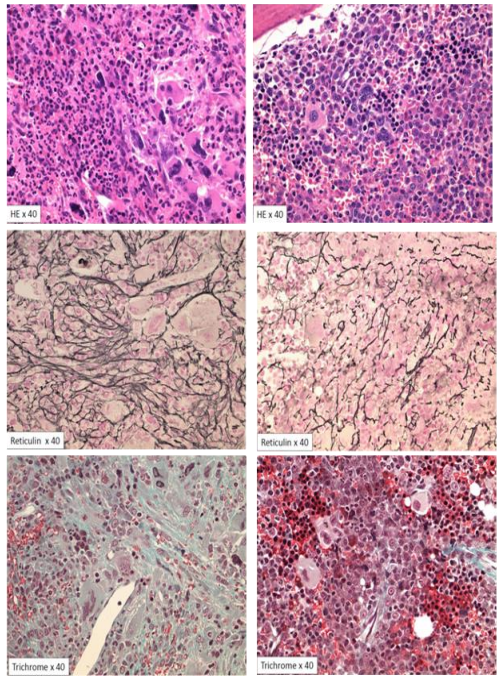
✓ **↓ TSS**



Fibrosis Changes

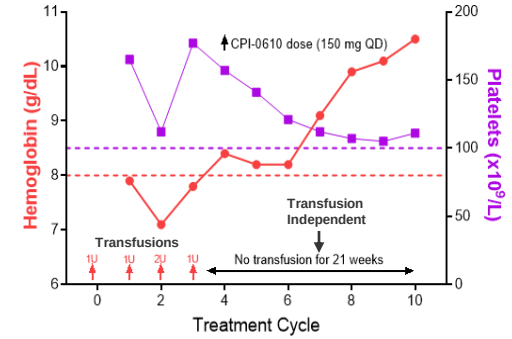
✓ **↓ Fibrosis, Δ Morphology**

Baseline	24-wks Post Tx
Gr 3 Fibrosis	**Gr 1 Fibrosis** (Focal Gr 2)
Megakaryocytic hyperplasia	Megakaryocytes: Normal distribution
Clusters erythroid hypoplasia	Relative erythroid hyperplasia

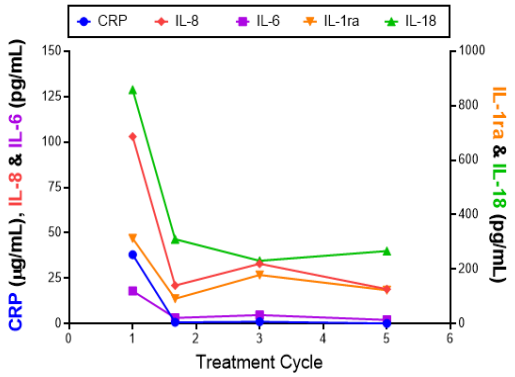


Hematologic and Molecular Effects

✓ **↑ Hgb**



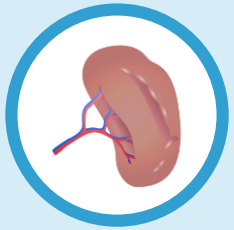
✓ **↓ Cytokines**



Notes: Transfusion-dependent JAK-Naïve patient. Extensive mutational burden - HMR = 2 (*ASXL1* and *SRSF2* mutations); Starting Dose CPI-0610 125mg QD+ Rux 10mg BID

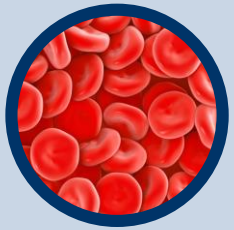
Working to Meet Unmet Needs for a Disease-Modifying Therapy That Impacts All Four Hallmarks of MF

Hallmarks of Myelofibrosis

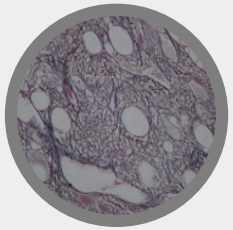


Spleen Volume

Constitutional Symptoms



Anemia & Transfusion Dependence



Bone Marrow Fibrosis

CPI-0610*

* Based on preliminary data as of April 17, 2020

Agenda

Topic	Presenter
• Company Profile • Overview of Myelofibrosis (MF) • Constellation's Vision for CPI-0610	• Jigar Raythatha
• MANIFEST Clinical Data	• Claire Harrison, D.M. (Oxon.)
• ***Regulatory Approval Pathway***	• ***Adrian Senderowicz, M.D.***
• Commercial Opportunity • Concluding Remarks	• Jigar Raythatha

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Proposed Global Pivotal Phase 3 Clinical Trial

Expected to Begin 2H 20

Study Population

JAK-inhibitor-naïve primary MF or post-ET/PV MF patients with:

- Advanced MF requiring therapy
- Splenomegaly
- Symptomatic

Design/Size

Double-Blind Randomization

Treatment Arm/Cohort

CPI-0610 + Ruxolitinib

Placebo + Ruxolitinib

Endpoints

- **Primary: SVR35 at 24 weeks**
- **Key Secondary: TSS50 by MFSAF v4.0 at 24 weeks**

ET = essential thrombocythemia PV = polycythemia vera SVR35 = ≥35% spleen volume reduction from baseline
TSS50 = ≥50% reduction in Total Symptom Score by MFSAF v4.0 = Myelofibrosis Symptom Assessment Form version 4.0

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Agenda

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• ***Commercial Opportunity*** • ***Concluding Remarks***	• ***Jigar Raythatha***

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CPI-0610 Potential Patient Opportunity

~40,000 Diagnosed Myelofibrosis Patients Worldwide

Low Risk/ Asymptomatic	Intermediate- and High-Risk

Don't Start Rux	Start/Continue Rux	Stop Rux

Rux Patient Population

Start CPI-0610/Rux	Add CPI-0610 to Rux Therapy	Stop Rux Start CPI-0610

CPI-0610 Addressable Patient Opportunity

Potential for CPI-0610 to Become Part of New Standard of Care and Expand the MF Opportunity

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Key Takeaways

- CPI-0610 in combination with ruxolitinib or as monotherapy showed preliminary evidence of clinical activity and potential disease modifying effects
- No evidence of correlation between SVR35 response and baseline risk status, platelet count, or spleen volume
- CPI-0610 as monotherapy and in combination with ruxolitinib was generally well tolerated
- Proceeding to initiate Phase 3 study in 2H 2020
- Potential to transform standard of care in MF

Note: April 17, 2020 Data Cutoff
SVR35 response = ≥35% spleen volume reduction from baseline

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Q&A